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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/722,689	11/24/2003	Mario Stevenson	UMY-034	3913

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EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/722,689	STEVENSON ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44 and 75-94* is/are pending in the application.

4a) Of the above claim(s) *23-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22 and 75-94* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/16/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendments were received and entered on 7/16/07 and 8/14/07.

Claims 1-44 and 75-94 are pending. Claims 23-44 stand withdrawn from consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/17/06.

Claims 1-22 and 75-94 are under consideration in this Office Action.

This Action is NON-FINAL due to new grounds of rejection not necessitated by amendment.

Rejections not reiterated from the previous action are withdrawn.

Specification/Compliance with Sequence Rules

Applicant's amendments filed 8/14/07 placed the application in compliance with 37 CFR 1.821 through 1.825.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 22 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 22 is drawn to the genus of siRNA complexes comprising one or more proteins associated with an siRNA that can mediate RNA interference of an HIV genome portion. The only portion of the specification as filed that appears to support this genus is at page 6, lines 9-11, which states: "[t]he term "siRNA complex" refers to a complex of siRNA and proteins that recognize and degrade RNAs with a sequence sufficiently homologous to that of the siRNA." This passage appears to refer to DICER or similar endonucleases that use siRNA as a guide sequence in the process of cleaving target RNAs. However, the claim is not limited to such proteins and embraces complexes of siRNAs and any protein such as polylysine, histone, or protamine. The specification as filed does not support such complexes, so the claim as amended embraces new matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3, 8-11, 14-19, 22, 77-81, 84, 86-94 are rejected under 35 U.S.C. 102(a) as being anticipated by Park et al (Nucleic Acids Research. Supplement (2001), No. 1, pp. 219-20).

Park taught double stranded RNAs targeted to gag and env regions of HIV (see abstract, and Fig.1 on page 219). As noted by Park, the double stranded RNAs are processed to 21-23 nucleotide siRNAs by cells, so Park inherently taught siRNAs of these lengths. The RNAs that form the double stranded RNAs were generated by in vitro transcription of PCR products comprising SP6 or T7 promoters, see paragraph bridging pages 219 and 220. Accordingly, and pertinent to claims 9 and 10, the siRNAs meet both the "expressed" and "synthetic" limitations in these claims. In any event, there is no difference between "expressed" and "synthetic" siRNAs, absent some limitation that is available to only one of the two genuses. The siRNA is considered to attack all HIV RNA substrates, e.g. viral RNA before or during early events such as reverse transcriptase production or cDNA synthesis, and mRNA expressed from a proviral integrant.

The "expressed from a vector" limitation of claim 84, 86 and 87 does not affect the structure of the siRNA, and so it receives no patentable weight. Similarly, claims 88-93 are included in this rejection because although they recite structural requirements of a vector (e.g. the vector must encode a plurality of siRNAs), these vector structure requirements are given no patentable weight because the claims are drawn to "a small interfering RNA (siRNA)", and not to a vector. The particulars of the vector are not considered to have any effect on the structure of the claimed siRNA.

Claims 1-3, 8-11, 14-22, 77-81, 84, and 86-94 stand rejected under 35 U.S.C. 102(e) as being anticipated by McSwiggen (US 20030175950 A1).

McSwiggen taught RNA interference mediated inhibition of HIV env gene expression using short interfering RNA. The siRNA of the invention can be unmodified or chemically modified. The siRNA of the instant invention can be chemically synthesized, expressed from a vector or enzymatically synthesized. The instant invention also features various chemically modified synthetic short interfering RNA (siRNA) molecules capable of modulating HIV gene expression/activity in cells by RNA inference (RNAi). See paragraph 11.

In one embodiment, nucleic acid molecules of the invention that act as mediators of the RNA interference gene silencing response are double stranded RNA molecules. In another embodiment, the siRNA molecules of the invention consist of duplexes containing about 19, 20, 21, 22, 23, or 24 nucleotides. In yet another embodiment, siRNA molecules of the invention comprise duplexes with overhanging ends of 1-3 (i.e., 1, 2, or 3) nucleotides, for example 21 nucleotide duplexes with 19 base pairs and 2 nucleotide 3'-overhangs. These nucleotide overhangs in the antisense strand are optionally complimentary to the target sequence. See paragraph 28. The siRNA is considered to attack all HIV RNA substrates, e.g. viral RNA before or during early events such as reverse transcriptase production or cDNA synthesis, and mRNA expressed from a proviral integrant.

The embodiments described above are supported in provisional application 60/374,722 (see e.g. pages 3, 9-11, 22, 23, 43, 52-54, and 107-110).

The "expressed from a vector" limitation of claim 84, 86 and 87 does not affect the structure of the siRNA, and so it receives no patentable weight. Similarly, claims 88-93 are included in this rejection because although they recite structural requirements of a vector (e.g. the vector must encode a plurality of siRNAs), these vector structure requirements are given no patentable weight because the claims are drawn to "a small interfering RNA (siRNA)", and not to a vector. The particulars of the vector are not considered to have any effect on the structure of the claimed siRNA.

Response to Arguments

Applicant's arguments, and the Declaration of Mario Stevenson and Jean-Marc Jacque under 35 USC 131, filed 8/14/07 have been fully considered. The Declaration was sufficient to overcome the rejections over Lois-Caballe and over Engelke. The Declaration also overcame the rejection of claims 4-7, 75, 76, 82, and 83 over McSwiggen. However, Applicant's arguments and the Declaration were not persuasive regarding the rejection over McSwiggen of claims 1-3, 8-11, 14-22, 77-81, 84, and 86-94. Applicant argues that the Declaration removes McSwiggen as a prior art reference under 35 USC 103(e) because the portions of McSwiggen relied upon in the rejection are not supported in the 60/294,140 priority document. This is unpersuasive because McSwiggen also claims priority to provisional application 60/374,722, which provides

support at pages 3, 9-11, 22, 23, 43, 52-54, and 107-110 for the embodiments relied upon in the rejection. For this reason the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-11, 14-22, 75-84, and 86-94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Draper et al (US 5693535) in view of Tuschl et al (US 7056704).

Draper taught ribozymes targeting various conserved sites in HIV RNA such as LTR, nef, vif, tat and rev. See column 4, lines 1-3 and 10-15; and column 9, lines 57-66. Note that some of the vif-targeted ribozymes also target pol. See column 10, lines 43-45.

Draper did not teach siRNA.

Tuschl taught siRNAs of 21-24 nucleotides (preferably 21 nucleotides) that are structurally and functionally equivalent to dicer cleavage products of longer dsRNAs. See column 28, lines 15-17. The siRNAs may contain modified nucleotides (column 3, lines 36-44), and mismatches relative to the target sequence are allowed at the termini

of the siRNAs (column 28, lines 25-32), for example it is routine to include terminal TT dinucleotides regardless of the target sequence.

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute siRNAs of Tuschl for the ribozymes of Draper when targeting HIV RNA for degradation. One would have been motivated to do so because siRNAs are more potent than ribozymes. Tuschl et al stated that "siRNAs are extraordinarily powerful reagents for mediating gene silencing" and that "siRNAs are effective at concentrations that are several orders of magnitude below the concentrations applied in conventional antisense or ribozyme gene targeting experiments." See column 23, lines 15-20. One would have had a reasonable expectation of success because the target sites of Draper were selected on the basis of their availability for hybridization. See column 10, lines 13-23, and 52-63.

The "expressed from a vector" limitation of claim 84, 86 and 87 does not affect the structure of the siRNA, and so receives it no patentable weight. Similarly, claims 88-93 are included in this rejection because although they recite structural requirements of a vector (e.g. the vector must encode a plurality of siRNAs), these vector structure requirements are given no patentable weight because the claims are drawn to "a small interfering RNA (siRNA)", and not to a vector. The particulars of the vector are not considered to have any effect on the structure of the claimed siRNA, and so are given no patentable weight.

Claims 13, 14, and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Draper et al (US 5693535) and Tuschl et al (US 7056704) as applied to claims 1-11, 14-22, 75-84, and 86-94 above, and further in view of Svoboda et al (Biochem. Biophys. Res. Comm. 287: 1099-1104, 2001).

The teachings of Draper and Tuschl are summarized above and can be combined to render obvious siRNAs directed to portions of an HIV genome. The references did not explicitly disclose shRNAs.

Svoboda taught that shRNAs, expressed from plasmids, were just as effective as dsRNAs comprising separate strands. See abstract.

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute shRNA for siRNA in the invention of Draper as modified by Tuschl. MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). Furthermore, MPEP 2144.07 indicates that the selection of a known material based on its suitability for its intended use supports the determination of prima facie obviousness. See also Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945). Finally, the substitution of shRNA for siRNA would have yielded predictable results to one of ordinary skill in the art at the time of the invention, in view of the teachings of Svoboda. Thus the invention as a whole was prima facie obvious.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, J. Douglas Schultz, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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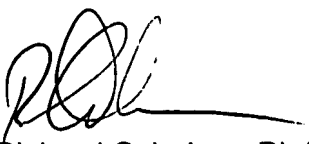

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